REMARKS

Claims 1-13, 15-29, 32-35,and 41-56 are currently pending. The Applicants appreciatively note that the Examiner has withdrawn the indefiniteness rejection presented in the last Office Action. The Examiner, however, maintains the enablement rejection.

I. Claims 1-13, 15-29,32-35, and 41-56 are rejected under 35 USC §112, ¶1 as allegedly failing to comply with the enablement requirement.

I. Claims 1-13, 15-29, 32-35, and 41-51 Are Enabled

The Examiner rejects Claims 1-13, 15-29, 32-35, and 41-51 because:

> ... the specification ... does not reasonably provide enablement for a transgenic non-human mammal ...

Office Action pg. 2. The Examiner maintains this rejection from the previous Office Action despite the fact that the Applicants previously argued that: i) one having ordinary skill in the art would be aware of the many reports in the art regarding the use of salivary regulatory genes to express proteins in a transgenic animal; ii) the specification discloses numerous salivary promoters and regulatory sequences that one having ordinary skill in the art could easily obtain; iii) that the prophetic examples are sufficiently enabling in view of the specification; and iv) the Applicant's have provided data showing the successful production of a transgenic non-human mammal capable of secreting a heterologous protein into saliva. On each point, the Examiner stated that the arguments were not persuasive. The Applicants disagree for the following reasons.

A. Samuelson Only Teaches PSP Minigene Limitations

The Examiner's cites Samuelson arguing that some salivary gland promoters may have limitations. The Applicants show that Samuelson only points to a small parotid salivary protein promoter construct (i.e., Lama) that exhibits limited expression:

> Smaller Psp transgenes containing varying amounts of 5'-flanking sequence fused to a Psp minigene were also expressed in the salivary gland; however, the level of expression in the parotid gland was only 1% of the endogenous gene levels (56)[1].

[1] Mikkelsen et al., Nucl Acid Res. 20:2249-2255 (1992), and discussed within Applicants' specification.

> ... Analysis of various 5' deletion constructs of the Psp minigene localized the position of critical transcriptional control sequences for basal expression in both parotid and SLG to a region between –4.6 kb and –3.1 kb. These results indicate that the minimal salivary-specific enhancer(s) are within 5 kb of the gene and that enhancer(s) for high level expression in the parotid are located elsewhere within the 25-kb cosmid clone.

Samuelson, pg 217 (emphasis added). Clearly, those skilled in the art recognized the limitation at the time and found the answer to eliminate the problem. Thus, based upon reading Samuelson, one having ordinary skill in the art would not be motivated to repeat Mikkelsen's minigene experiment using a Lama minigene and expect high level expression. Certainly, the Applicants did not. The Applicants specification contemplate using promoters that are 4.6 kB or larger. *See, Applicants' Specification pg 27 ln 15-16.*

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claims 1, 20, 29, and 52 to recite that the cis-transcriptional control elements of at least 4.6 kB. This amendment is made not to acquiesce to the Examiner's argument but only to further the Applicants' business interests, better define one embodiment and expedite the prosecution of this application.

B. Use Of bSP30 Promoters Do Not Require Undue Experimentation

Further, the Examiner objects to the data provided in the Erickson Declaration based on an argument that the use of the bSP30a and bSP30b promoter constructs are allegedly beyond the scope of the instant specification:

> However, the guidance provided by the specification does not correlate to use of any particular saliva specific regulatory element for the creation of transgenic non-human mammals embraced by the claims. Moreover, the guidance provided by the specification is general as it does not even disclose which saliva regulatory elements could be used to create any of the transgenic non-human mammals embraced by the claims. ... Given the lack of guidance provided by the specification it would have required undue experimentation ...

Office Action pg. 3. The Examiner does not explain what is meant by "undue experimentation". The mere fact that some experimentation may be necessary does not allow a conclusory statement that such experimentation is undue. In fact, the Federal Circuit has supported the United States Patent & Trademark Board of Appeals by stating that:

> The Board observed, that "the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would

> have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of vaccine preparation.

Falkner v. Inglis, 448 F.3d 1357, 1365 (Fed. Cir. 2006). Here, the Examiner has not shown the presence of 'undue experimentation'. In fact, the Examiner has relied upon Samuelson to allegedly show 'undue experimentation' whereas the Applicants have demonstrated that Samuelson admits that apparent high level expression problems regarding the PSP minigenes were readily recognized and solved (*supra*).

C. Incorporation By Reference Is Not Required For A Known Gene Sequence

In addition, the Examiner has insisted that the allegedly undisclosed regulatory sequences are "essential" thereby requiring a proper incorporation by reference of the allegedly missing information:

> Finally, in an attempt to provide guidance as to which saliva regulatory sequence may be used within the scope of the claimed invention, the specification has relied on improper incorporation by reference of subject matter that appears to be essential.

Office Action pg. 4. Again, the Applicants disagree because the Federal Circuit has held otherwise:

> With respect to a skilled artisan's ability to identify "essential" poxvirus genes ... as of the time of filing ... professional journals had disclosed the DNA sequence of the poxvirus genome along with the locations of the "essential regions". The person of ordinary skill in the art would clearly have possessed such knowledge, and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic. Indeed, "[a] patent need not teach, and preferably omits, what is well known in the art." *Spectra-Physics, Inc. v. Coherent, Inc. 827 F.2d 1524, 1534 (Fed. Cir. 1987).*

Falkner v. Inglis, 448 F.3d 1357, 1365 (Fed. Cir. 2006). Clearly, DNA sequences that have been publically available at the time of filing of a patent application need not be included in the patent application and can be relied upon for enablement. This case law, alone, is sufficient to require the Examiner to withdraw the present enablement rejection.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants provide a Declaration from Dr. Thomas Wheeler that: i) the sequences of BSP30a and BSP30b were known in the art at the time of filing, and were classified as parotid secretory proteins (PSPs). See, 37 CFR §1.132 "Declaration of Dr. T. Wheeler (hereinafter, "The Wheeler Declaration"). The Examiner is requested to note that the sequences of both the

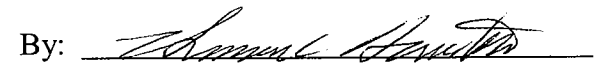
bSP30a (Tab A) and the bSP30b (Tab B) amino acid and nucleic acid sequences were made available to the public by Dr. Wheeler with a 1996 posting to GeneBank. *See, The Wheeler Declaration, ¶ 2.* In parallel with these sequence postings Dr. Wheeler published a 1996 paper related to bSP30 protein that not only disclosed partial amino acid sequences, but more importantly, concluded that bSP30 was not a proline-rich protein thereby suggesting that the protein most more likely related to the parotid salivary proteins. Further, the 1996 Wheeler paper explicitly stated that high level bSP30 protein expression was due to genetic differences in the pSP30 promoter between the high and low bloat cattle lines. *See, The Wheeler Declaration, ¶ 3.* Dr. Wheeler's further work confirmed the specuation that the bSP30 protein was, indeed, a parotid secretory protein. *See, The Wheeler Declaration, ¶ 4.* Consequently, in 1996 (six years before the application was filed) one having skill in the art did know that the bSP30 gene was likely related to the parotid secretory protein family and the amino acid and nucleotide sequences had been published.

The Applicants believe that the present application meets and/or exceeds all the enablement requirements as interpreted by the Federal Circuit. Consequently, the Examiner is now respectfully requested to withdraw the rejection and allow the pending claims.

CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect at 617.984.0616.

Dated: March 21, 2008

By: 

Thomas C. Howerton
Registration No. 48,650

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, CA 94105
617.984.0616